

REMARKS

Claims 1-18 are pending in this application. All of the pending claims stand rejected and claims 3, 4, and 11-13 have been objected to because of certain informalities. This Reply amends claims 3, 4, 11, and 12, and addresses each of the objections and rejections raised in the Office Action mailed March 19, 2001. Applicants respectfully request reconsideration of the pending claims in view of the amendments and the following remarks.

Claim Amendments

Claims 3, 4, 11, and 12 have been amended to correct certain informalities in the claims in order to overcome the objections raised by the Examiner. The changes to the claims are formal in nature and are not related to the scope of the claimed invention. No new matter is added by these amendments.

Claim Objections

Claims 3, 4, and 11-13 have been objected to under 37 C.F.R. § 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. In particular, the Examiner contends that these claims read on the "hydrogel" composition of claim 1, but claim 1 is directed to a "hydrogel precursor." The Examiner further objects to claim 4 because it depends on claim 11 when it should dependent on claim 1. Claim 11 is also objected to because it refers to a molecule, yet no molecule is recited in its base claim (claim 9).

Applicants have amended the claims to correct the defects identified by the Examiner. Specifically, claims 3, 4, 11, and 12 have been amended to refer to a hydrogel. Claims 4 and 11 have been further amended to correct the identity of the base claims from which they depend. In light of these amendments, the objections to these claims may now be withdrawn.

With respect to claim 13, Applicants note that this claim depends from claim 2, which is directed not only to a precursor, but recites a “hydrogel or hydrogel precursor composition.” Thus, the reference in claim 13 to a “hydrogel” is proper and the objection to this claim should be withdrawn.

Rejection under 35 U.S.C. § 102

Claims 1, 5, and 9 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Amiel et al. The Examiner asserts that Amiel discloses hydrophobically end-capped polyethylene oxide and water-soluble β -cyclodextrin polymers. The Examiner contends that such disclosure contemplates a hydrogel precursor comprising a polymer and a protecting group, and thus meets the limitations of claims 1, 5 and 9. Applicants respectfully traverse this rejection.

Amiel describes an associating system that involves mixing hydrophobically end-capped polyethylene oxide (PEO) with a water soluble β -cyclodextrin polymer in aqueous solution. Amiel, however, does not describe the use of cyclodextrins as protecting groups to inhibit gel formation. Although Amiel uses the interaction between hydrophobic groups and cyclodextrin molecules to control the state of the polymer gel, Amiel uses

cyclodextrins in a very different way than the use provided by the present invention. In Amiel, the cyclodextrin groups are used as polymerizing groups to induce the formation of a gel. Amiel discloses that the reported thickening properties of the composition are due to polymolecular associations that result from the formation of an inclusion complex between the PEO terminal groups and β -cyclodextrin. As Amiel explains:

[T]he appearance of thickening properties ...[is] due to polymolecular associations.... The β -cyclodextrin polymers are promoting the associations between the amphiphilic polymer by forming inclusion complexes between the hydrophobic moieties and the β -cyclodextrin cavities.

Id. at 61 (emphasis added). Amiel repeatedly emphasizes that the formation of these inclusion complexes between the hydrophobic PEO terminal groups and the β -cyclodextrin cavities “are at the origin of the polymolecular associations.” *Id.*

By contrast, in the present invention, the cyclodextrins are used as protecting groups to prevent the gelling of the hydrogel precursor. Indeed, claim 1 specifically recites “a physical chemical protecting group preventing gel formation of said hydrogel precursor composition” (emphasis added). Thus, cyclodextrins are used in the present invention for the opposite purpose for which they are used by Amiel.

Furthermore, the hydrophobically end-capped PEO chains described in Amiel are not capable of assembling into a gel until the cyclodextrins are added. Amiel measured the specific viscosity of the modified PEO and reported that “no thickening effects have been observed.” *Id.* at 64. It was not until the PEO polymer was mixed with the cyclodextrin polymer that Amiel reports a thickening effect was obtained. (See bottom of p. 64 and Figure 2). By comparison, claim 1 of the instant application recites that the

polymer component of the composition is “capable of assembling into a hydrogel under physiological conditions.”

In sum, Amiel describes the use of a *polymer* of cyclodextrins to **promote** formation of a gel. The claimed invention uses *single* cyclodextrins to **prevent** a gel from forming. Thus, the present invention uses cyclodextrin to achieve a very different result from that described by Amiel. Indeed, Amiel seeks the opposite result. Furthermore, the modified PEO polymer described in Amiel is unable to form a gel until the cyclodextrin is added. In contrast, the polymer component of the present invention is capable of assembling into a gel under physiological conditions, in the absence of cyclodextrin or another protecting group. For these reasons, Applicants respectfully submit that claims 1, 5, and 9 are not anticipated by Amiel, and the § 102 rejection should be withdrawn.

Rejection Under 35 U.S.C. § 103

Claims 1-18 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Amiel et al. in view of Hedstrand et al., Rhee et al., and Jodal et al. Applicants respectfully traverse this rejection.

The secondary references are cited as teaching certain limitations recited in the dependent claims and to demonstrate that it would have been within the capability of one skilled in the art to make the present invention. For example, the Examiner asserts that Rhee demonstrates that biological molecules (such as cyclodextrin) can be attached to polymers (such as PEG); Hedstrand teaches that hydrophobic groups can be attached to

the tips of polymers, including branched polymers; and Jodal discloses that cyclodextrin can be degraded by α -amylase. Although these observations by the Examiner are correct, the secondary references do not compensate for the deficiencies of Amiel. As discussed in detail above, Amiel uses cyclodextrin molecules to form a gel, not to prevent a gel from forming. None of the secondary references teach or suggest the use of cyclodextrin as a protecting group to inhibit gel formation.

Furthermore, since Amiel uses cyclodextrin molecules to induce gelling, if one skilled in the art combined the gel of Amiel with the teachings of Rhee, Hedstrand, and Jodal, the cyclodextrin would not be used as a protecting group and thus the α -amylase would not function as a deprotecting group. Instead, since the cyclodextrin would be used to form the gel, the addition of the α -amylase enzyme would have exactly the opposite effect as that intended: it would cause the gel to degrade.

Since the secondary references fail to provide the key teachings that are lacking from Amiel (i.e., use of a protecting group, such as cyclodextrin, to prevent gel formation), even in combination, the cited references do not render the claimed invention obvious. The § 103 rejection should, therefore, be withdrawn.

CONCLUSION

In light of the foregoing amendments and remarks, Applicants submit that the claims are now in condition for allowance and such action is respectfully requested. Enclosed is a petition to extend the period for replying for two months, to and including August 20, 2001, as August 19, 2001 falls on a Sunday. Also enclosed is a check in the

amount to cover the cost of the petition. If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date:

August 20, 2001

Timothy J. Douros
for Kristina Bieker-Brady, Ph.D.

Reg. No. 39,109

Reg. No. 41,716

Clark & Elbing LLP

176 Federal Street

Boston, MA 02110

Telephone: 617-428-0200

Facsimile: 617-428-7045

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Version with markings to show changes made

Claims 3, 4, 11 and 12 have been amended as follows:

3. (Amended) The [hydrogel or] hydrogel precursor composition of claim 1, wherein said polymer domain comprises poly(ethylene glycol), poly(vinyl alcohol), poly(vinyl pyrrolidone), poly(ethyl oxazoline), poly(acrylic acid), poly(acrylamide), poly(styrene sulfonate), poly(amino acids), polysaccharides, or copolymers thereof.

4. (Amended) The [hydrogel or] hydrogel precursor composition of claim [11]1, wherein said chemical protecting group is β -cyclodextrin.

11. (Amended) The [hydrogel or] hydrogel precursor composition of claim [9]10, wherein said molecule that covalently binds to said hydrophobic interacting groups is hydrophilic.

12. (Amended) The [hydrogel or] hydrogel precursor composition of claim 1, wherein said polymer domain comprises poly(ethylene glycol) and said hydrophobic interacting groups are perfluorinated hydrocarbons.